REMARKS

Claims 13, 15-16, and 18-22 have been canceled without prejudice or disclaimer. Applicants reserve the right to file one or more continuation or divisional applications directed to the canceled subject matter. New claims 23-28 have been added. New claim 23 corresponds to original claim 13, new claim 24 corresponds to original claim 16, new claim 25 corresponds to orgianl claim 16, new claim 26 corresponds to original claim 20, new claim 27 corresponds to orginal claim 22. Basis for new claim 28 can be found in claim 24, orginal claim 15 and the specification at pages 7-8, bridging paragraph and example 1. No new matter has been added. Entry and reconsideration is respectfully requested.

The rejection of claims 13-22, as it now pertains to new claims 23-28 and original claims 14 and 17 under 35 USC 103(a) as being unpatentable over Guthrie et al, United States Patent Application US2001/0055627 is respectfully traversed. The Office states that original claims 13-15 are drawn to a method of reducing the level of apolipoprotein B production comprising administering an effective amount of a polymethoxyflavone. It then states that claims 16-22, are drawn to polymethoxyflavone compositions suitable for reducing the level of apolipoprotein B.

The Office further states that Guthrie teaches that flavonoids, including polymethyoxyflavones such as nobiletin and tangeretin inhibit LDL cholesterol and apolipoprotein B (apo-B) synthesis, and are thus effective for reducing atherosclerosis, hypercholesterolemia, and lowering the risk of cardiovascular disease. The Office states that Guthrie further teaches that apolipoprotein B is the principal protein of LDL and that the binding of apo-B to LDL receptors results in internalization and degradation of LDL, promoting clearance of LDL from plasma and regulating intracellular cholesterol handling. The Office states that Guthrie does not teach all of the polymethoxyflavones claimed and that Guthrie does teach flavones/flavonoids broadly for the use of reducing apo-B levels, as well as those specific polymethoxyflavones such as nobiletin and tangeretin. As such, applicants's use of polymethoxyflavones which are members of the broad class recited in Guthrie for the same purpose of reducing apo-B levels is encompassed by the teachings of Guthrie. The Office goes on to state that applicant has set forth compositions wherein known polymethoxyflavones are combined for reducing the level of substances which contribute to cardiovascular diseases or disorders stating that the combination of two compounds known to acheive the same effect in a composition is seen as obvious,

unless there is some unexpected result. The Office states that the prior art has clearly set forth the use of specifically claimed polymethoxyflavones, and the class of flavones/flavonoids broadly as agents effective in reducing apo-B and that the combination of these agents into a composition would be obvious. The Office concludes that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to use a polymethoxyflavone in a composition for reducing the level of apolipoprotein B. It further concludes that a person of ordinary skill in the art would have been motivated to use polymethoxyflavones in a composition for reducing the level of apolipoprotein B given that the prior art has set forth flavones, specifically polymethoxyflavones, act as agents which reduce the level of apolipoprotein B and LDL cholesterol whcih consequently reduces the incidence of cardiovascular diseases, atherosclerosis, or hypercholesterolemia.

Applicants respectfully submit that the Guthrie patent fails to motivate one of ordinary skill in the art to practice the instantly claimed invention, especially as the Office pointed out, the Guthrie reference does not specifically teach that the claimed polymethoxyflavones in a method for reducing levels of

apolipoprotein B. Furthermore, the reference does not teach the class of flavone/falvonoids broadly as agents effective in reducing apo-B. At page 1, paragraph 2, third sentence from the last sentence, the application states: " The invention further relates to the identification of compounds of liminoids, flavonoids, and trocotrienols that have the specific inhibitory effects on synthesis of liver cholesteryl esters and/or degradation of apo-B". The compounds of the instantly claimed invention are not identified by the published patent application. The published patent application specifically teaches that hesperetin, tangeretin, and naringenin reduced apo-B levels. There are no other teachings in the published patent application which teach any other compounds for reducing levels of apo-B.

The Office is using the improper standard of obvious to try. It is respectfully submitted that the essence of obviousness does not arise by merely picking and choosing from the prior art to produce the claimed invention. "In order to establish *prima facie* obviousness it is necessary for the examiner to present evidence preferably in the form of some teaching, suggestion, incentive, or general available knowledge, that one of ordinary skill in the art would have been led to combine relevant teachings of the applied references in the proposed manner to

arrive at the claimed invention. Ex parte Levengood, 28 USPQ2d 1300, 1301 (Bd. Pat. & Int'f, 1993). Starting from this correct standard of obviousness, the error of the Office is clear-the rejection is improper because the Office has failed to identify any teachings in the prior art motivating the skilled artisan to to produce the method and compositions of the presently claimed invention. No references or combination of references have been provided which would teach, suggest, or motivate one of ordinary skill in the art to modify the Guthrie et al. application to use the polymethoxyflavones of the instantly claimed invention to reduce apolipoprotein B production. There is simply no motivation save for the teachings of the inventor's application, to produce the claimed invention. The Office is also using the improper standard of ***IMPROPER*** hindsight analysis. It is impermissible to use the claimed invention as an instruction manual or template to piece together the teachings of the prior art so that the claimed invention is rendered obvious. One cannot use improper hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention. The Guthrie et al. application fails to render the instantly claimed invention *prima facie* obvious.

Therefore, Applicant respectfully submits that no *prima*

facie case of obviousness has been established and the instant rejection be withdrawn.

In the event this paper is deemed not timely filed, the undersigned petitions for an appropriate extension of time. Please charge any fees which may be required by this paper or at any time during prosecution of the instant application, or credit any overpayment, to deposit account 50-2134.

Respectfully Submitted

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DATE

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CERTIFICATE OF FILING VIA FACSIMILE

The undersigned hereby certifies that the attached **Amendment After Final Rejection (11 pages) and Notice of Appeal (2 copies)** were this day August 20,2003 filed in the United States Patent and Trademark Office via facsimile to facsimile number 703-308-4556 Pages: 14

Gail E. Poulos